DEPARTMENT OF HEALTH & HUMAN SERVICES

San Francisco District
1431 Harbor Bay Parkway
Alameda, CA 94502-7070
Telephone: 510/337-6700

WARNING LETTER

VIA FEDERAL EXPRESS

November 29, 2006

James D. Merselis
President and CEO
HemoSense, Inc.
651 River Oak Parkway
San Jose, CA 95134-1907

Dear Mr. Merselis:

During an inspection of your firm located in San Jose, California on May 15, 2006 through July 13, 2006, investigators from the United States Food and Drug Administration (FDA) determined that your firm manufactures the INRatio INR System, an in vitro diagnostic system that provides a quantitative prothrombin time value with the use of fresh capillary whole blood. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 321(h), these products are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or are intended to affect the structure or function of the body.

This inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act (21 U.S.C. § 351(h)), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (C.F.R.), Part 820. We received your response dated July 27, 2006, and an August 30, 2006, from Mr. Doug Rundle, Vice President, Quality Assurance and Regulatory Affairs, concerning our investigator's observations noted on the Form FDA 483, List of Inspectional Observations that was issued to you. We address your response below, in relation to each of the noted violations. These violations include, but are not limited to, the following:

1. Failure of management with executive responsibility of ensuring that quality system requirements are effectively established and effectively maintained as required in 21 C.F.R. 820.20(b)(3)(i).

   For example:

   - Quality audits failed to identify deviations in complaint handling.
   - Devices not meeting performance specifications are not being investigated.
   - Products labeled and distributed with the wrong strip code were not investigated.

We have reviewed your responses and have concluded that they are inadequate because your corrective and preventive actions to address the specific observation have not been completed. Please provide the District Office with a copy of your root cause analysis and your corrective action(s) in the prevention of this quality deviation.

2. Failure to investigate complaints involving the possible failure of a device, labeling, or packaging to meet any of its specifications as required in 21 C.F.R. 820.198(c).

For example:

- Complaint #[redacted] The date of the event and the date your firm received the complaint was February 7, 2006. The complaint involved discrepant results between the INRatio INR device ([redacted]) and the Lab INR ([redacted]). No investigation was performed because the packaged identified an expiration date of January 31, 2006; however, the strips were validated to meet specifications up to a 15 months shelf life from the manufactured date. The package represents a 12 month shelf life and although you are aware of your 15 month validation data, you failed to perform an investigation.

- Complaint #[redacted]: The date of the event and the date your firm received the complaint was April 28, 2006. A "Professional" user reported an InRatio INR device reading of [redacted], which is "Way off". No investigation was performed because the package identified an expiration date of March 31, 2006. However, your validation study demonstrates a shelf life of 15 months, and you failed to perform an investigation.

- Complaint #[redacted]. The date of the event and the date your firm received the complaint was March 1, 2006. The complaint involved discrepant results in two patients as follows:

  1. Patient #[redacted]: InRatio INR of [redacted]; Retest identified [redacted]; and another Retest identified [redacted]

  2. Patient #[redacted]: InRation INR of [redacted]; Retest identified [redacted]

  The complaint was not reviewed until May 14, 2006, and your firm determined that an investigation was not required as the packaged identified an expiration date of April 30, 2006.

We have reviewed your responses and have concluded that they are inadequate because your corrective and preventative action is not completed. The effectiveness of your actions will be evaluated during our follow-up investigation.

3. Failure to promptly review, evaluate, and investigate complaints representing events that are MDR reportable under 21 CFR Part 803, as required in 21 C.F.R. 820.198(d).

For example:

- Complaint #[redacted] was received on December 21, 2005. On December 18, 2005, patient's INRatio = [redacted], however, [redacted] sample contained [redacted] and patient was [redacted] from various sites. The physician ordered lab test and Lab INR = [redacted]. On

February 14, 2006, your firm determined that an investigation was needed; as of our inspection date of May 15, 2006, an investigation had not been performed.

- Complaint #[redacted] was received on September 9, 2005. On September 7, 2005, patient's INRatio =[redacted]. The patient experienced[redacted] and[redacted] and was admitted to the hospital with an INRatio =[redacted]. On January 19, 2006, your firm determined that an investigation was needed; however, an investigation was not performed until March 28, 2006, 200 days from the receipt of the compliant.

- Complaint #[redacted] received on March 1, 2006. On February 14, 2006, patient's INRatio =[redacted]. The patient started[redacted] from the[redacted] and[redacted]. The subject was admitted to the hospital with an INRatio =[redacted] and the patient[redacted]. On April 7, 2006, your firm determined that an investigation was required, but did not perform one because the "strips" lot number was not provided.

We have reviewed your responses and have concluded that it is inadequate because your corrective and preventive action is not completed and FDA has not evaluated the effectiveness of your actions. We acknowledge your firm's commitment to complete the investigations for complaint numbers[redacted] and[redacted]

4. Failure to investigate the cause of nonconformities relating to product, processes, and the quality system as required in 21 C.F.R. 820.100(a)(2).

For example: Over[redacted] INRation Test Strips were labeled with the wrong strip code. The purpose of the strip code is to set the meters variable in its calculation of the INR. You opened a NCMR (Non-conforming Material Report) number[redacted] on February 27, 2006 to investigate the cause. On March 24, 2006 the NCMR was closed; however, no investigation into the cause of the nonconformity was performed.

We have reviewed your responses and have concluded that they are inadequate because it is unclear whether a failure investigation was performed to determine the root cause of this quality deviation. In addition, your responses do not indicate whether a corrective and preventive action was initiated to prevent the recurrence of releasing strips with the wrong code.

5. Failure to ensure that all personnel are trained to adequately perform their assigned responsibilities as required in 21 C.F.R. 820.25(b).

For example:

- The following were not investigated per SOP[redacted]. Complaint numbers[redacted]

- The following complaints were not filed within 30-days as required by SOP[redacted] Complaint numbers[redacted]

We have reviewed your responses and have concluded that it is inadequate. Your responses states that you have conducted additional training with appropriate personnel. It is unknown if a root cause analysis was performed to identify the cause of the non-

conformity. Retraining your employees may not correct and/or prevent the recurrence of this observation because you might not know the root cause. It is your responsibility to determine the cause of this quality failure and develop a corrective and preventive action plan to prevent its recurrence. The effectiveness of your corrective action(s) will be evaluated during our follow-up investigation.

Based on our review of your responses, we find that retraining your employees was required in five of the eight observations noted on the Form FDA-483. It is your responsibility to establish procedures for identifying training needs and to ensure that all personnel are trained to adequately perform their assigned responsibilities as required in 21 C.F.R. 820.25(b).

Our inspection also revealed that your INRatio INR devices are misbranded under section 502(t)(2) of the Act, 21 U.S.C. 352(t)(2), in that your firm failed or refused to furnish material or information respecting the device that is required by or under section 519 of the Act, 21 U.S.C. 360i, and 21 C.F.R. Part 803 - Medical Device Reporting (MDR) regulation. Significant deviations include, but are not limited to, the following:

Failure to report, within 30 days of receiving or otherwise becoming aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer: (1) may have caused or contributed to a death or serious injury; or (2) has malfunctioned and such device or a similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur as required in 21 CFR 803.50(a).

For example:

- Complaint [redacted] received on December 21, 2005. On December 18, 2005, the patient's INRatio = [redacted] for which patient's [redacted] sample contained [redacted] and the patient was [redacted] from more than one site. Patient was admitted to hospital and the Lab INR = [redacted] The MDR reportable event was submitted to the FDA on February 3, 2006, over 40 days after the receipt of the complaint.

- Complaint [redacted] received on December 19, 2005. On that day, the patient's INRatio = [redacted] with a retest of [redacted]. The complaint was identified as a discrepant result, meeting your MDR reporting requirement to file a "product malfunction" report. An MDR event report was submitted to the FDA on April 17, 2006, over 115 days after the receipt of the complaint.

- Complaint [redacted] received on March 2, 2006. Patient's INRatio = [redacted] and the Lab INR = [redacted]. This value exceeded the 95% confidence limit of [redacted]. This event represents a device malfunction similar to that in Complaint [redacted] (received March 1, 2006) that also exceeded the 95% confidence limit. That malfunction event resulted in a death and a MDR reportable event was filed within 30-days. However, this similar event was not filed until April 11, 2006, over 38 days after the receipt of the complaint.

We have reviewed your responses and have concluded that they are inadequate because sufficient details and documentation of your root cause analysis were not provided for us to evaluate whether your preventive actions are adequate to prevent the recurrence of the observation.

You should take prompt action to correct the violation(s) addressed in this letter. Failure to promptly correct these violation(s) may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties. Also, federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, premarket approval applications for Class III devices to which the Quality System regulation deviations are reasonably related will not be approved until the violations have been corrected. Requests for Certificates to Foreign Governments will not be granted until the violations related to the subject devices have been corrected.

Please notify this office in writing within fifteen (15) working days from the date you receive this letter of the specific steps you have taken to correct the noted violations, including an explanation of how you plan to prevent these violation(s), or similar violation(s), from occurring again. Include documentation of the corrective action you have taken. If your planned corrections will occur over time, please include a timetable for implementation of those corrections. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to: Lawton W. Lum, Compliance Officer, 1431 Harbor Bay Parkway, Alameda, California 94502. If you have any questions about the content of this letter please contact him at 510-337-6792.

Finally, you should know that this letter is not intended to be an all-inclusive list of the violation(s) at your facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violation(s) noted in this letter and in the Inspectional Observations, Form FDA 483 (FDA 483), issued at the closeout of the inspection may be symptomatic of serious problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violation(s), and take prompt actions to correct the violation(s) and to bring your products into compliance.

Sincerely yours,

Joseph P. Ibsen for

Barbara J. Cassens
District Director